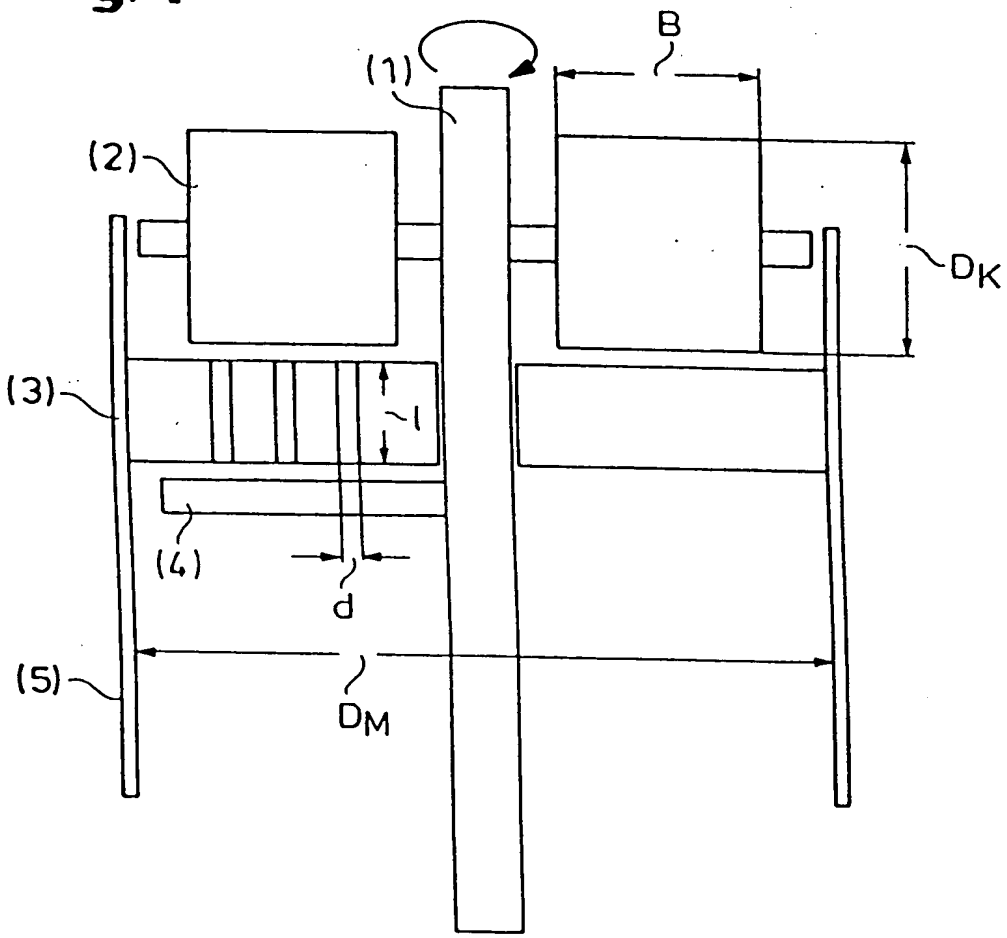**Fig. 1**